spacing of the lines was such that it made reading and entry of amendments difficult. The substitute specification is a verbatim copy of the original specification as filed, except for typographical errors that have been corrected as indicated above. No new matter is, thus, introduced with the substitute specification. Page numbers and line numbers describing the amendments in the specification refer to page numbers and line numbers in the substitute specification.

Claim 1 has been amended to make explicit that the enhancing amount of DHA and ARA is administered to preterm infants by adding these compounds to a nutritional product for preterm infants or to a nutritional supplement for said infants. Support for the amendment can be found in Application, page 5, lines 27-30 of the substitute specification.

Claim 2 has been amended to make explicit that DHA and ARA are supplemented into preterm infant formula. Preterm infant formulas are referred to in the body of Claim 14. In addition, one example of preterm infant formula, Enfamil® Premature Formula, is cited at page 5, line 17, of the substitute specification as one of the formulas that can be used to practice the present invention. Consequently, the amendment does not introduce any new matter.

Claim 14 has been amended to remove the term "suitable" that was objected as indefinite by the Examiner. As amended, the preamble of Claim 14 reads: "An infant formula for preterm infants". The body of the claim already recited an improvement of a "preterm infant formula". Consequently, the amendment does not introduce any new matter.

A. Claim Rejections under 35 U.S.C.§ 112

The Examiner rejected Claims 14-20, under 35 U.S.C. § 112, second paragraph asserting that the presence of the term "suitable" in Claim 14 rendered this claim and those that depended on it (Claims 15-20) indefinite. Per the Examiner, "suitable" is a relative term and the specification does not provide a standard to measure the required degree of suitableness.

Claim 14 is now amended and the objected term removed. Applicants respectfully submit that Claims 14-20 are definite, and request the Examiner to withdraw this rejection.

B. Claim Rejections under 35 U.S.C. § 102

The Examiner rejected Claims 1,3, and 4 under 35 U.S.C. § 102(b) as anticipated by the established common practice of breast-feeding premature infants, in view of the teachings in the publication by Crozier et al. and U.S. Patent No. 5,374,657 to Kyle. Per the Examiner, Crozier et al. discloses that breast milk contains sufficient amounts of DHA and ARA to help premature infants, and Kyle teaches that the ARA-to-DHA ratio in human milk is about 3:1. Because a 3:1 ratio is within the ranges for the ARA-to-DHA ratio claimed in Claims 3-4, the Examiner concludes that Claims 1, and 3-4 read on breast-feeding premature infants. Applicants respectfully submit that this rejection under 35 U.S.C. § 102(b) is improper.

Specifically, to anticipate a claim, a single reference must contain all of the elements of the claim. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628,631,

2USPQ2d 1051, 1053 (Fed Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.") (Emphasis added). Missing elements may not be supplied by the knowledge of one skilled in the art or the disclosure of another reference. *Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 716, 223 USPQ 1261, 1271 (Fed. Cir. 1984). Where a reference discloses less than all of the claimed elements, an examiner may only rely on 35 U.S.C. §103. *Titanium Metals*, 778 F2d 775, 780, 227 USPQ 773,777 (Fed. Cir. 1985). Therefore, because the Examiner utilizes three references for rejecting Claims 1, 3 and 4, it is respectfully submitted that the rejections be withdrawn.

In any event, if the §102(b) rejections were proper, Claim 1, as amended, makes explicit that the growth enhancing amount of ARA and DHA is administered to preterm infants by adding those compounds to nutritional products and nutritional supplements for preterm infants. Thus, the rejected claims can no longer be interpreted as reading on breast-feeding premature infants. Consequently, Applicants respectfully request the Examiner to withdraw the rejections for this substantive reason as well.

The Examiner also rejected, under 35 U.S.C. § 102(b), Claims 14-16 and 18-19 as anticipated by U.S. Patent No. 5,374,657 to Kyle in view of the publication by Crozier et al. For the same reasons as discussed above, Applicants respectfully submit that the rejection of these claims under 35 U.S.C. § 102(b) is improperly based on two references. In any event, Applicants respectfully submit, the Examiner's substantive analysis is incorrect.

Per the Examiner, Kyle teaches an infant formula comprising DHA and ARA in amounts comparable to those present in human milk. The Examiner asserts that the ARA/DHA ratio and the concentration of those compounds in human milk are within the ranges claimed in the rejected claims. The Examiner admits that Kyle's formula is not for preterm infants, however, but fails to recognize that, with this admission, the Examiner also admits that the Kyle's product (formula for term infants) is not the product (improved formula for preterm infants) of the present invention.

Formulas for term infants, as the formula in Kyle, are different to formulas for preterm infants, because the nutritional needs of those two groups of infants are also different. Specifically, before birth, the fetus receives its nutritional needs, including DHA and ARA, through the placenta. Prematurely born infants need those same nutrients, in quantity and quality, as if they were still in the womb, regardless of the levels of those nutrients that may be present in the mother's milk at the time of the premature birth. There is no necessary correlation between the nutrient levels in the preterm mother's milk and the preterm infant's needs. These needs are not met, either, by formulas designed for term infants. In short, Kyle's formula is not the formula of the present invention. Applicants respectfully request the Examiner to withdraw this rejection.

C. Claim Rejections under 35 U.S.C. § 103

The Examiner also rejected claims 1-8, 16 and 20, under 35 U.S.C. § 103(a), as being unpatentable over Kyle in view of Crozier et al. The Examiner asserts that Kyle teaches an infant formula comprising DHA and ARA in comparable amounts as in human milk. The Examiner further asserts that the ARA/DHA ratio in human milk is

about 3:1 to 2:1 and cites in support of those numbers Kyle's examples in column 13-16, and Kyle's claims. Applicants disagree. The examples show only that the ARA/DHA ratio in human milk is 3:1. That Kyle claims a range from 3:1 to 2:1 shows only that Kyle's formula contains that ARA/DHA ratio, not that that is the ratio in human milk. And Kyle's formula, again, is a formula for term infants.

The Examiner also asserts that Kyle teaches that ARA and DHA is critical for a healthy growth of infants. The Examiner admits that Kyle addresses term infants' needs and that Kyle does not teach the administration of the formula to preterm infants. However, the Examiner states that Crozier et al. teach that ARA and DHA are "particularly important for preterm infants to proper growth and development". Thus, the Examiner concludes, "it would have been prima facie obvious to a person of ordinary skill in the art . . . to employ the infant formula of Kyle for feeding preterm infants." Applicants respectfully submit that the Examiner is mistaken.

As discussed in a previous section, term infants' nutritional needs are substantially different to those of preterm infants. No one skilled in the art would suggest to feed formulas designed for term infants to preterm infants. The nutritional "golden standard" for feeding term infants, i.e., human milk, does not apply to preterm infants. Thus, it is not obvious to feed Kyle's formula to preterm infants. To the contrary, feeding term formula to preterm infants would be a nutritional mistake.

Furthermore, there is no motivation in Crozier et al. to add DHA and ARA to preterm formulas to enhance the preterm infants' growth. Crozier et al.'s teachings regarding "proper growth and development of the preterm infant" are not what the Examiner interprets. Specifically, on page 95, column 2, lines 1-11, the authors discuss

the new understanding of the scientific community regarding the role that lipids have in cell structure and function. One aspect of this understanding, "is the contribution of nutritionally essential fatty acids to growth and function of nervous tissue in the infant." (Emphasis supplied)

The authors then proceed to focus on the two particular acids at the center of this invention: docosahexaenoic acid (DHA) and arachidonic acid (ARA). On page 96, column 3, lines 1-22, the authors explain:

> Both docosahexaenoic and arachidonic acids are important in brain growth. Brain tissue is 60% lipid and its fatty acid composition is surprisingly constant: the predominant acids are AA [ARA] and DHA.

After discussing the preterm infants' inability to synthesize DHA and ARA from their fatty acid precursors, the authors continue to explain the role of these essential fatty acids. At page 97, column 2, lines 1-21, the authors discuss the apparent effect of these acids on visual function and brain development:

> Breast-feeding has an effect on maturation of visual acuity. Measures of visual evoked potential and forced-choice preferential looking were significantly different in infants fed breast milk compared to those fed formulas. Measures of intellectual development have also been demonstrably different between breast and formula fed preterm infants. Morley et al showed that preterm infants who had been given breast milk had better developmental scores at the age of 18 months. This advantage continued: at 7.5 to 8 years of age, the breast-fed group scored significantly higher intelligence quotients as demonstrated by the Weschler Intelligence Scale for Children.

These quoted paragraphs clearly show that for Crozier et al. "proper growth and development of the preterm infants" means "proper growth of the nervous system and mental development of the preterm infant." Preterm infants' proper brain growth, accelerated maturation of visual acuity, and improved intellectual development are the benefits that the authors seek in promoting the

addition of DHA and ARA to infants' formula. The authors, unlike Applicants, do not seek to increase the rate of weight gain in preterm infants or teach that such an increase is possible by feeding the infants DHA and ARA.

The authors of the article do not suggest that the addition of those fatty acids to the infants' food may have the effect of enhancing the infants' weight gain. To the contrary, Carlson et al.'s study found a significant drop in the studied infants' weight gain when the infants were fed with DHA from fish oil. The authors postulated that eicosapentaenoic acid (EPA), an acid that was present in the fish oil studied at an EPA to DHA ratio of 1.5:1 which competes with ARA in many biochemical reactions, may substitute for ARA in those reactions and, thus, may be responsible for the drop in weight gain. There is no suggestion or indication in Crozier et al. that the addition of ARA be made for purposes other than compensating for the drop in weight gain observed by Carlson et al. There is no teaching in Crozier et al. that an effect other than compensating for that drop in weight gain is even possible.

The present invention, on the other hand, rests on the surprising discovery that adding DHA and ARA to a preterm infant formula not only cancels the drop in weight gain reported by Carlson et al. but also increases the weight gain to such an extent that preterm infants receiving DHA & ARA enhanced formula during their one-month hospitalization after birth and who are then switched to regular term infant formula without DHA or ARA after discharge from the hospital have, after 57 weeks from conception, approximately the same weight as term infants continuously breast-fed since birth.

The above-referred surprising result of Applicants' investigation is clearly shown in the Application. Specifically, in the Final Study Report, under the heading Study Objective and Statistical Analysis, Application, page 22, lines 16-29 (approximately), Applicants report the goals of their investigation as follows;

> The primary objective of this study was to establish the safety of feeding D [DHA-enhanced formula] or DA [DHA & ARA-enhanced formula] to preterm infants during the initial hospitalization as measured 1) by growth, acceptance and tolerance while consuming the formula for at least 1 month and 2) by close monitoring and observation for a 4 to 5 month follow-up period (4-5 times the treatment period) while consuming unsupplemented routine term infant formula. The primary growth parameter selected was weight with evaluation of the proposition that weight on test formula was greater than or equal to weight on control formula.
>
> ...
>
> Secondary objectives were 1) to evaluate the impact of fatty acid levels in erythrocyte phospholipids at the end of study feeding and 2) to determine if any effect on mean visual acuity greater than half an octave could be demonstrated at 2 and 4 months corrected age. (Emphasis supplied)

Further, at page 23, lines 7-13 of the Application, Applicants report the results as follows:

> Post-hoc analysis reveals that infants on DA [DHA & ARA-enhanced formula] grew faster than infants receiving C [regular formula] and D [DHA-enhanced formula] (See table 5 and figure 1). This enhanced growth provided faster "premature infant catch-up" compared to C and D. Weight achieved by the DA group (3198 g) was higher than C (3075 g) and D (3051 g) at 40 weeks post-conceptual age but had not fully caught up to the term weight (3438 g) of group H [breast-fed term infants] (See table 4 and figure 2). This catch up trend continued through 48 to 57 weeks by which time the mean weight of group DA did not differ from group H while groups C and D remained significantly lower.

These surprising results, wholly unexpected from the teachings in Crozier at al., clearly show that the claimed method enhances the preterm infant physical growth beyond levels achievable with formulas not supplemented with both DHA and ARA. Without these results, the person with ordinary skill in the art finds no

motivation to administer formulas containing DHA and ARA to preterm infants to enhance their weight gain beyond the levels achievable with unsupplemented formulas. Thus, we respectfully submit that the claimed method to enhance preterm infants' growth by administering a growth-enhancing amount of DHA and ARA is patentable over the references cited by the Examiner.

The Examiner, however, did not consider Applicants' arguments, asserting that the Examiner needs not "appreciate the difference between 'proper growth' in the prior art and 'enhanced growth'." The Examiner postulates that the "enhancing growth" requirement of the claims in the present application need not be given patentable weight because the recitation occurs in the preamble. Applicants respectfully submit that the Examiner is mistaken.

Specifically, the requirement of "enhancing growth" does not occur only in the preamble of a claim. While claim 1 preamble recites a "method for enhancing the growth of preterm infants", the same claim, in its body, teaches the administration to preterm infants of "a growth enhancing amount of DHA and ARA." Furthermore, claim 14 recites an improved infant formula for preterm infants wherein the improvement comprises the addition to the formula of "a growth enhancing amount of DHA and ARA." This expression, "growth enhancing amount of DHA and ARA", appearing in the body of claims 1 and 14, is defined in the specification. Applicants respectfully submit that the term must be given patentable weight and that, by doing so, the present invention is patentably distinct over the references cited by the Examiner.

In summary, in view of the foregoing arguments, we respectfully submit that the rejected claims are patentably distinct over the references cited by the Examiner and meet all other statutory requirements. We believe that the present Application is now in complete condition for allowance and, therefore, respectfully request the Examiner to reconsider the rejections in the Final Office Action and allow this Application. We invite the Examiner to telephone the undersigned should any issues remain after the consideration of this response.

Please charge any additional fees that may be required to Deposit Account No. 50-2548.

Respectfully requested,

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Version With Markings Showing Changes To The Amended Claims

1. A method for enhancing the growth of preterm infants comprising administering to said infants a growth enhancing amount of DHA and ARA wherein the DHA and ARA are added into nutritional products or nutritional supplements for preterm infants.

2. The method of Claim 1 wherein DHA and ARA are supplemented into preterm infant formula.

14. An infant formula [suitable] for [enhancing the growth of] preterm infants, the improvement comprising the inclusion in said preterm infant formula of a growth enhancing amount of DHA and ARA.